REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-9 are pending in this application, and claims 1-5 are rejected. Claims 6-9 were withdrawn as non-elected subject matter.

Claim 1 has been amended to recite that "the polypeptide is obtained by deleting amino acids 1 to 47 of cGMP-dependent protein kinase Iα (PKG Iα)." Support for this language can be found in the specification, for example, at page 6, lines 12-15, page 11, lines 8-9 (Example 1) and original claims 2-3. Other editorial changes have been effected which are self-explanatory.

Therefore, no new matter has been added by this amendment.

Claims 2-3 have been canceled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any canceled subject matter.

Claims 1 and 4-9 are now pending in this application.

II. FOREIGN PRIORITY DATE

Kindly acknowledge the claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

III. REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 2 and 3 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the reasons set forth at page 2, lines 3-13 of the Office Action.

The present amendment cancels the rejected claims, thereby rendering the rejection moot.

IV. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

Claims 1-5 were rejected under 35 U.S.C. § 112, first paragraph, for a lack of written description support for "the genus of fusion proteins" the reasons set forth on pages 2-3 of the Office Action.

This rejection is respectfully traversed as applied to the amended claims for the following reasons.

The test for sufficiency of written description is whether the disclosure of the application reasonably conveys to the artisan that the inventor had possession at the time of filing of the subject matter which is claimed. This requirement may be satisfied by: (1) a reduction to practice; (2) a reduction to drawings/chemical formulas; (3) a disclosure of relevant identifying characteristics, such as structure or other physical and/or chemical properties, to describe the claimed invention in full, clear, concise and exact terms; (4) a disclosure of functional characteristics coupled with a known or disclosed correlation between function and structure sufficient; (5) a sufficient description of a representative number of species; or (6) a combination of the above. See M.P.E.P. § 2163, 2100-170 to 2100-174, II, A, 3 a(i)-(ii).

The amended claims are directed to a cGMP-visualizing probe comprising a polypeptide that specifically binds cGMP and is obtained by deleting amino acids 1 to 47 of cGMP-dependent protein kinase Iα (PKG Iα (Δ1-47)) and two chromophores with different fluorescence wavelengths, which are linked to the N-terminal and C-terminal of the polypeptide.

The specification, in particular Example 1 at page 10, line 20 to page 11, line 19, and Figure 1, describes the preparation of at least five fusion proteins corresponding to the present invention. The specification at pages 6-8 also defines the functional domains of the cGMP-binding proteins. Moreover, Example 1 at page 11, lines 11-19, discloses the preparation of a cGMP-visualizing probes comprising cyan fluorescent protein (CFP) + PKG Iα (Δ1-47) + yellow fluorescent protein (YFP), corresponding to the amended claim invention. See also Figure 1. On page 3, lines 15-17

of the Office Action, it is acknowledged that the specification is enabling for this fusion protein. Clearly, such disclosure amounts to a reduction to practice of the claimed invention.

Accordingly, one of skill in the art, upon reading the specification would reasonably conclude that the Applicants had possession of the invention as claimed. Therefore, in view of the above, the rejection of claims of 1-5 under 35 U.S.C. § 112, first paragraph, is untenable and should be withdrawn.

V. REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH ENABLEMENT

Claims 1-5 were rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification is only enabling for a cGMP probe consisting of two chromophores capable of exhibiting FRET and residues 48-671 of cGMP-dependent kinase Iα or the A12 mutant of cGMP-dependent kinase Iα and optionally linker peptides between said chromophores and cGMP binding peptide. See pages 3-6 of the Office Action.

This rejection is respectfully traversed for the same reasons set forth above with respect to the written description rejection of claims 1-5 and for the following reasons.

The test of enablement is whether one reasonably skilled in the art could make or use the invention based on the disclosure in the specification coupled with information known in the art without undue experimentation. See M.P.E.P. § 2164.01.

As noted above, Example 1 at page 10, line 20 to page 11, line 19, and Figure 1, describes the preparation of at least five fusion proteins corresponding to the claimed invention. The specification at pages 6-8 also defines the functional domains of the cGMP-binding proteins. Moreover, Example 1 at page 11, lines 11-19, discloses the preparation of the claimed cGMP-visualizing probes comprising CFP + PKG Iα (Δ1-47) + YFP. See also Figure 1. The amino acid sequence of PKG Iα is known in the art. Accordingly, the amended claims are directed to an embodiment indicated as enabled by the Examiner on page 3 of the Office Action.

Furthermore, attached are the following three articles as further support that the specification is enabled for the claimed invention:

1. Romoser et al., J. Biol. Chem., vol. 272, no. 20, pp. 13270-13274 (1997);
2. Mizuno et al., Biochem., vol. 40, pp. 2502-2510 (2001); and
3. Karasawa et al., J. Biochem., vol. 381, pp. 307-312 (2004).

These articles describe various chromophores capable of exhibiting FRET.

For instance, Romoser discloses fluorescent indicator composed of two GFP variants joined by a calmodulin-binding domain from smooth muscle myosin light chain kinase. Romoser, page 12370, Abstract.

Mizuno discloses the biochemical and biophysical properties of a red fluorescent protein from *Discosoma* species (DsRed). Mizuno demonstrated the fluorescence resonance energy transfer (FRET) between *Aequorea* GFP variants and DsRed. Mizuno created chimeric proteins (cameleons) containing YFP, cyan fluorescent protein (CFP) or Sapphire as the donor and RFP as the acceptor. Mizuno, page 2502, Abstract.

Karasawa discloses the molecular cloning and characterization of two fluorescent proteins (Fps) as FRET donors, i.e., CFP (cyan FP) and an orange FP. Karasawa, page 307, 1st column, Introduction, last paragraph. Karasawa also discusses the use of the GFP and a red FP (DsRed). Karasawa, page 307, 1st column, Introduction, 1st paragraph; Figure 1, page 308.

Thus, these articles demonstrate that chromophores other than CFP and YFP are well known and may be used in the probes. In this regard, it is well established that a specification need not teach, and preferably omits, what is well known in the arts. M.P.E.P. § 2164.01.

Also, as described and demonstrated in the Example 5, at page 14, lines 1-14, linker peptides are optional.

Thus, upon reading the disclosure, one skilled in the art could make or use the amended claimed invention based on the disclosure in the specification coupled with information known in the art without undue experimentation.

In view of the above, the rejection of claims 1-5 under 35 U.S.C. § 112, first paragraph, for a lack of enablement, is untenable and should be withdrawn.

VI. REJECTIONS UNDER 35 U.S.C. § 102

A. Honda or Sato

Claims 1-5 were rejected under 35 U.S.C. § 102(a) as anticipated by Honda et al. (AO) or Sato et al. (AN), both cited in the form PTO-1449, submitted March 4, 2002. See page 7 of the Office Action.

This rejection is respectfully traversed for the following reasons.

Enclosed is an English translation of the foreign priority document, thereby perfecting the foreign priority date of July 4, 2000. The publication dates of the Honda and Sato references are February 27, 2001 and December 13, 2000, respectively, which are after the priority date of the present application, namely, July 4, 2000. Thus, Honda and Sato are removed as prior art references. Accordingly, the rejection of claims 1-5 under 35 U.S.C. § 102(a) is untenable and should be withdrawn.

B. Tsien

Claims 1-4 were rejected under 35 U.S.C. § 102(b) as anticipated by Tsien et al., U.S. Patent No. 5,998,204, cited in a previous form PTO-1449. See page 8.

To anticipate a claim, a cited prior art reference must either expressly or inherently teach each and every element of the claimed invention. See M.P.E.P. § 2131.01.

Again, the amended claims are directed to a cGMP-visualizing probe comprising a polypeptide that specifically binds cGMP and is obtained by deleting amino acids 1 to 47 of cGMP-dependent protein kinase Iα (PKG Iα (Δ1-47)) and two chromophores with different fluorescence wavelengths, which are linked to the N-terminal and C-terminal of the polypeptide.

Tsien fails to disclose or suggest a polypeptide obtained by deleting amino acids 1-47 of PKG Iα. In other words, Tsien fails to disclose or suggest the PKG Iα (Δ1-47) peptide.

For this reason, Tsien cannot be said to teach or suggest each and every element of the amended claimed invention. Thus, Tsien fails to anticipate the claimed invention.

In view of the above, the rejection of claims 1-5 under 35 U.S.C. § 102(b) is untenable and should be withdrawn.

VII. REJECTION UNDER 35 U.S.C. § 103

Claim 5 was rejected under 35 U.S.C. § 103(a) as obvious over Tsien et al. in view of Zhao et al., cited in the form PTO-892. See page 8.

To establish obviousness, three criteria must be met. First, the prior art references must teach or suggest each and every element of the claimed invention. Second, there must be some suggestion or motivation in the references to either modify or combine the reference teachings to arrive at the claimed invention. Third, the prior art must provide a reasonable expectation of success.

This rejection is respectfully traversed for the same reasons set forth above regarding the Tsien reference and for the following reasons. Specifically, the cited prior art fails to disclose or suggest each and every element of the claimed invention, namely, the PKG Iα (Δ1-47) polypeptide.

As noted Tsien fails to disclose or suggest the PKG Iα (Δ1-47) polypeptide. Similarly, Zhao also fails to disclose or suggest this polypeptide. Yet, as indicated in the Example section, when PKG Iα (Δ1-47) is used as the cGMP binding peptide in the probe, detection and quantification of cGMP are achieved with high responsiveness and accuracy.

For this reason, Tsien and Zhao cannot be said to disclose or suggest each and every element of the amended claimed invention. Thus, Tsien and Zhao fail to render obvious the amended claimed invention.

In view of the above, the rejection of claims 1-5 under 35 U.S.C. § 103(a) is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is now in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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November 16, 2004

THE COMMISSIONER IS AUTHORIZED TO CHARGE ANY DEFICIENCY IN THE FEES FOR THIS PAPER TO DEPOSIT ACCOUNT NO. 23-0975

ATTACHMENTS TO AMENDMENT AND REPLY:

1. Romoser et al., J. Biol. Chem., vol. 272, no. 20, pp. 13270-13274 (1997);
2. Mizuno et al., Biochem., vol. 40, pp. 2502-2510 (2001);
3. Karasawa et al., J. Biochem., vol. 381, pp. 307-312 (2004); and
4. English translation of the foreign priority document, JP-2000-202730.